Portal Vein Thrombosis in a Chirrotic Patient with Immune Thrombocytopenic Purpura During Eltrombopag Treatment

İmmün Trombositopenik Purpuralı Sirozlu Bir Hastada Eltrombopag Tedavisi Sırasında Portal Ven Trombozu

Portal Vein Thrombosis due to Eltrombopag

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Özet

Portal ven trombozu karaciğer sirozunda görülen nadir ancak ciddi bir komplikasyondur. Eltrombopag immün trombositopenide kullanılan ikinci jenerasyon bir ajandır. Trombotik komplikasyonlara yol açabilmektedir. Portal ven trombozu eltrombopag kullanılan bazı siroz hastalarında nadir rapor edilen yaşamı tehdit eden bir komplikasyondur. Burada eltrombopag kullanımı sonrası portal ven trombozu gelişen 63 yaşındaki immün trombositopenik bir siroz vakası sunulmuştur.

Anahtar Kelimeler

Portal Ven Trombozu; İmmün Trombositopenik Purpura; Eltrombopag

Abstract

Portal vein thrombosis (PVT) is a rare but serious complication in liver cirrhosis. Eltrombopag is a new, second generation agent used for immune thrombocytopenic purpura (ITP). It may cause thrombotic events. PVT has been rarely reported as a life threatening complication in some cirrhotic patients during eltrombopag using. We presented 63 years old cirrhotic and immune thrombocytopenic patient who had PVT after eltrombopag.

Keywords

Portal Vein Thrombosis; Immune Thrombocytopenia; Eltrombopag

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Introduction

Eltrombopag is a second generation thrombopoietin receptor agonist used for immune thrombocytopenic purpura in last years. Some studies showed that it increased deep vein and pulmonary thrombosis risk while platelet count was normal or subnormal [1].

Portal vein thrombosis (PVT) is a life threatening event caused by myeloproliferative diseases, cirrhosis, cancer and infections. It occurs acutely or chronically. Clinical features of PVT is ranged from asymptomatic disease to gastrointestinal bleeding and acute intestinal ischemia. PVT is rare but life threatining complication showed in patients with chronic liver disease and thrombocytopenia during eltrombopag treatment [2,3,4].

In cirrhotic patints, PVT frequency is 0,6-15,8%. Hereditary or aquired thrombophilic factors, bacterial infections and reduced portal vein flow increase frequency. In cirrhosis both procoagulant and anticiagulant factors decrease and coagulation balance can move to one side easily. There are some studies showing increase in factor 8 and decrease in protein C in these patients. Factor V leiden, prothrombin and methylenetetrahydrofolate mutations have minimal importance on PVT. While in case of partial PVT, patients are asymptomatic, in case of full obstruction, acute abdomen and lombar pain may occur. Bloodless diarrhea can be seen if there is additional mesenteric vein thrombosis. Patients with chronic PVT can be asymptomatic or can be diagnosed with symptoms of hypersplenism or portal hypertension. Cavernous transformation of portal veins or hepatopedal collateral veins can be seen. Doopler ultrasonography or ultrasonography are generally sufficient for diagnosis but computarizated thomography or magnetic resonance are more sensitive for showing extension of thrombus in detail. Anticoagulation must be done in acute PVT. The aim is recanalization of veins and prevention of intestinal enfarction and portal hypertension.

Antithrombin III, TIPS (transjugular intrahepatic portosystemic shunting) are other treatment options. Therapy of chronic PVT is controversial. If thrombophilic factors or risk of mesenteric vein extension are available, therapy should be made. TIPS can be made too [5].

Here we reported portal vein thrombosis case with Child A cirrhosis and ITP treated with Eltrombopag.

Case Report

A 63 years old male patient with Child A cirrhosis of unknown etiology was admitted to our clinic with hemorrhage in the mouth. His platelet count was 2400/μL, hemoglobin and leukocyte were 8,5 g/dl and 3400/ μL. His basal platelet count was 50 000-55 000/μL and in peripheral blood smear there were rare, single thrombocytes. Bone marrow was hypercellular and number of megakaryocytes was normal. Anti HBV, anti HCV, anti HIV antibodies and anti nuclear antibody were negative. We gave him 1000 mg/day of metil prednisolon for 5 days with immune thrombocytopenia diagnosis. Because his platelet count didn'nt rise, we started intravenous 1 g/kg/day (60 g/day) of immunoglobulin for 2 days. After that we continued the treatment with oral 1 mg/kg/day (64mg/day) of metil prednisolon for one month. His platelet count rised up to 10 000/μL and oral bleeding continued. And then we added azatiopurine 50 mg two times a day. He had ear bleeding. He took azatiopurin for 1 month and platelet count reached only up to 18000/μL. He rejected splenectomy operation. For this reason we decided to stop azatiopurin and gave him eltrombopag with low dose (15 mg/kg/day). After one month platelet count reached to 97000/μL but he complained of abdomen and back pain. Portal venous doppler ultrasonography showed ascites and thrombus in portal vein extending right main branch at intrahepatic region and in splenic veins. We gave low dose (3500 units/day) bemiparins sodium subcutaneously to him. For 3 months ,he is being followed with about 50 000/ μL platelet count.

Discussion

Trombocytopenia is seen approximately 49-64% in chronic liver disease patients. Platelet levels rarely decrease under 30 000-40 000/μL. Thrombocytopenia causes are hypersplenism, impaired thrombocyte production, immune or no immune factors. Immune thrombocytopenia is seen more frequently due to hepatit C [6].

In a phase II study, 74 HCV-related cirrhosis patients were given eltrombopag at doses of 30,50 and 75 mg/day. Platelet counts of patients were 20-70 000/μL. Most of patients reached to platelet count of 100 000/μL at 4 week [7].

Portal vein thrombosis after eltrombopag has been reported as a rare but mortal complication. Treatment and prognosis are not clear because of few number of cases.

Two PVT cases were reported in two cirrhotic patients. One of them was with eltrombopag, another one was with romiplostim. In two cases, treatment was stopped and anticoagulant therapy was given and thrombosis of them were resolved [3,4].

In a randomised study, 75 mg/kg eltrombopag was given to 145 chronic liver patient at dose of 75 mg daily for 14 days before invazive procedures. Platelet requirment was 28% in eltrombopag group vs 81% of placebo group. PVT was seen in 6 patients who recieved eltrombopag as compared with 1 who recieved placebo. Study was finished early [7].

In a patient with HCV related cirrhosis and ITP, low dose (12,5 mg/day) eltrombopag was used. Fifty four days later portal vein thrombosis occured. Althoug eltrombopag was stopped, subsequently pulmonary and deep vein thrombosis were shown. Heparin and antithrombin III were used and recanalization was seen. [8]. In our case, thrombosis occured in portal and splenic veins at the first month of the treatment. Immediately, we stopped eltrombopag and started low molecular wight heparin. We had used eltrombopag with low dose but couldn't prevent thrombosis.

Mechanism of thrombosis development with eltrombopag is not clear. Increase in platelet count and activity can be causes [8].

In non cirrhotic patients, standart treatment of PVT is anticoagulation with drugs such as antithrombin III and heparin for 14-15 months. But in cirrhotic patients, anticoagulant therapy increased bleeding [7]. In a cirrhosis case with PVT after eltrombopag, there was no bleeding [8]. In these kinds of patients, treatment must be set for each patient individually.

In conclusion, our case and other cases show that eltrombopag may cause PVT which is a letal complication in chronic liver disease. Therefore, in such patients eltrombopag must be used carefully and endication of this drug must be evaluated with randomised studies.

Competing interests

The authors declare that they have no competing interests.

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